

WHAT IS CLAIMED IS:

- 1 1. An isolated nucleic acid molecule encoding a replication competent recombinant
2 Hepatitis C Virus (HCV) genome, which nucleic acid comprises all or part of an HCV
3 genome and is able to replicate efficiently when transfected into a susceptible cell line
4 without reducing the growth rate of said cell line by more than 10 fold.
- 1 2. The isolated nucleic acid molecule encoding a recombinant HCV genome of claim 1,
2 which nucleic acid comprises from 5' to 3' on the positive-sense nucleic acid
3 (a) a functional 5' HCV non-translated region (NTR) comprising an extreme
4 5'-terminal conserved sequence;
5 (b) at least one open reading frame (ORF) encoding a heterologous gene
6 operatively associated with an expression control sequence, wherein the
7 heterologous gene and expression control sequence are oriented on the
8 positive-strand nucleic acid molecule;
9 (c) an ORF encoding at least a portion of an HCV polyprotein whose cleavage
10 products form functional components of HCV virus particles and RNA
11 replication machinery, and
12 (d) an HCV 3' NTR comprising an extreme 3'-terminal conserved sequence,
13 and wherein said nucleic acid is able to replicate efficiently in a susceptible
14 cell line without reducing the growth rate of said cell line by more than 10
15 fold.
- 1 3. The isolated nucleic acid of claim 1, wherein the susceptible cell line is selected from
2 the group consisting of human hepatoma cell line Huh-7, human hepatoma cell line
3 HepG2, hepatoma cell line PH5CH, *T. belangeri* liver cell line MBTL, human diploid
4 fibroblast cell line VERO, secondary monkey kidney cell line CV-1, T cell line MT-2,
5 T cell line HPBMa10-2, T cell line MOLT-4, and B cell line Daudi.

- 1 4. The susceptible cell line of claim 4, which is human hepatoma cell line Huh-7.

- 1 5. The isolated nucleic acid molecule according to claim 1, which is selected from the
 2 group consisting of double stranded DNA, single stranded DNA, double stranded
 3 RNA, and single stranded RNA.

- 1 6. An isolated nucleic acid molecule which is not more than 99.9% identical and is at
 2 least 95% identical to SEQ ID NO: 1.

- 1 7. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
 2 HCVR 2 (SEQ ID NO: 2).

- 1 8. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
 2 HCVR 8 (SEQ ID NO: 3).

- 1 9. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
 2 HCVR 9 (SEQ ID NO: 4).

- 1 10. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
 2 HCVR 22 (SEQ ID NO: 5).

- 1 11. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
 2 HCVR 24 (SEQ ID NO: 6).

- 1 12. A stable cell line transfected with the isolated nucleic acid molecule according to
 2 claim 1, wherein said cell line:

- 3 (a) has a growth rate which is not less than 10% of the growth rate of the
4 corresponding naïve cell line, and
5 (b) is capable of supporting efficient replication of said isolated nucleic acid.

1 13. The cell line of claim 12 wherein said cell line is selected from the group consisting of
2 human hepatoma cell line Huh-7, human hepatoma cell line HepG2, hepatoma cell
3 line PH5CH, *T. belangeri* liver cell line MBTL, human diploid fibroblast cell line
4 VERO, secondary monkey kidney cell line CV-1, T cell line MT-2, T cell line
5 HPBMa10-2, T cell line MOLT-4, and B cell line Daudi.

1 14. The cell line of claim 12 wherein said cell line is derived from a human hepatoma cell
2 line Huh-7.

1 15. The cell line of claim 14 designated HCVR 2 and having ATCC Accession No. PTA-
2 2489.

1 16. The cell line of claim 14 designated HCVR 8 and having ATCC Accession No. PTA-
2 2490.

1 17. The cell line of claim 14 designated HCVR 9 and having ATCC Accession No. PTA-
2 2486.

1 18. The cell line of claim 14 designated HCVR 22 and having ATCC Accession No.
2 PTA-2487.

1 19. The cell line of claim 14 designated HCVR 24 and having ATCC Accession No.
2 PTA-2488.

20. A method of screening for anti-HCV therapeutics, which method comprises comparing a level of HCV subgenomic replicon RNA or replicon RNA-associated protein expression in the cell line of claim 12 contacted with a candidate therapeutic agent to the cell line not contacted with the candidate therapeutic agent, wherein a decrease in the level of HCV subgenomic replicon RNA or replicon RNA-associated protein expression is indicative of the inhibitory activity of the agent.

21. A method for detecting antibodies to HCV in a biological sample from a subject comprising contacting said sample with the protein fractions derived from the cell line of claim 12 under conditions that permit interaction of HCV-specific antibodies in the sample with the HCV protein(s) produced in said cell line, followed by detecting binding of the antibodies in the sample to these HCV-derived protein(s), wherein said binding is indicative of the presence of HCV infection in the subject from which the sample was derived.

1 22. The method of claim 21 wherein said biological sample is selected from the group
2 consisting of blood, serum, plasma, blood cells, lymphocytes, and liver cells.